

# Refine Search

## Search Results -

Terms	Documents
6627427.pn.	1

Database:

US Pre-Grant Publication Full-Text Database  
US Patents Full-Text Database  
US OCR Full-Text Database  
EPO Abstracts Database  
JPO Abstracts Database  
Derwent World Patents Index  
IBM Technical Disclosure Bulletins

Search:

L5

Refine Search

Recall Text

Clear

Interrupt

## Search History

DATE: Friday, March 10, 2006 [Printable Copy](#) [Create Case](#)

### Set Name Query

side by side

### Hit Count Set Name

result set

DB=USPT; PLUR=YES; OP=OR

L5 6627427.pn.

1 L5

DB=PGPB; PLUR=YES; OP=OR

L4 L1 and (AT specific for ethylmalonyl)

1 L4

L3 L1 and (KSQ domain)

1 L3

L2 L1 and (loading module)

1 L2

L1 20030235892

1 L1

END OF SEARCH HISTORY

# Hit List

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## Search Results - Record(s) 1 through 10 of 91 returned.

### ☐ 1. Document ID: US 7008636 B2

L12: Entry 1 of 91

File: USPT

Mar 7, 2006

US-PAT-NO: 7008636

DOCUMENT-IDENTIFIER: US 7008636 B2

TITLE: 2,3,5-substituted biphenyls useful in the treatment of insulin resistance and hyperglycemia

DATE-ISSUED: March 7, 2006

PRIOR-PUBLICATION:

DOC-ID

DATE

US 20040214869 A1

October 28, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Butera; John A.	Clarksburg	NJ		US
Caufield; Craig E.	New York	NY		US
Graceffa; Russell F.	Hampton	NH		US
Greenfield; Alexander	Princeton Junction	NJ		US
Gundersen; Eric G.	Plainsboro	NJ		US
Havran; Lisa Marie	Bordentown	NJ		US
Katz; Alan H.	Lawrenceville	NJ		US
Lennox; Joseph R.	Morrisville	NC		US
Mayer; Scott C.	Robbinsville	NJ		US
McDevitt; Robert E.	Somerset	NJ		US

US-CL-CURRENT: [424/433](#); [514/354](#), [514/396](#), [514/415](#), [514/416](#), [514/469](#), [514/571](#); [546/339](#), [548/335.1](#), [548/469](#), [548/470](#), [549/471](#), [562/512](#), [562/587](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	KMC	Draw Desc	Ima
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### ☐ 2. Document ID: US 7001735 B2

L12: Entry 2 of 91

File: USPT

Feb 21, 2006

US-PAT-NO: 7001735

DOCUMENT-IDENTIFIER: US 7001735 B2

TITLE: Glucose transporter/sensor protein and uses thereof

DATE-ISSUED: February 21, 2006

PRIOR-PUBLICATION:

DOC-ID

DATE

US 20020038464 A1

March 28, 2002

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Charron; Maureen J.	Flushing	NY		US
Katz; Ellen B.	Port Washington	NY		US

US-CL-CURRENT: 435/7.23; 435/6, 435/7.1, 436/64

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	KMC	Draw Desc	Ima
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☐ 3. Document ID: US 6959048 B1

L12: Entry 3 of 91

File: USPT

Oct 25, 2005

US-PAT-NO: 6959048

DOCUMENT-IDENTIFIER: US 6959048 B1

TITLE: Optimizing link quality by space and time interleaving

DATE-ISSUED: October 25, 2005

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Horneman; Kari	Oulu			FI
Katz; Marcos	Oulu			FI
Ylitalo; Juha	Oulu			FI

US-CL-CURRENT: 375/299; 455/101, 455/103

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	KMC	Draw Desc	Ima
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☐ 4. Document ID: US 6921650 B1

L12: Entry 4 of 91

File: USPT

Jul 26, 2005

US-PAT-NO: 6921650

DOCUMENT-IDENTIFIER: US 6921650 B1

TITLE: Recombinant methods and materials for producing epothilone and epothilone derivatives

DATE-ISSUED: July 26, 2005

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Julien; Bryan	Oakland	CA		
Katz; Leonard	Hayward	CA		
Khosla; Chaitan	Palo Alto	CA		
Tang; Li	Foster City	CA		
Ziermann; Rainer	San Mateo	CA		

US-CL-CURRENT: 435/76; 435/252.31, 435/252.33, 536/23.1, 536/23.2, 536/23.7

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	KMC	Draw Desc	Ima
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☐ 5. Document ID: US 6894639 B1

L12: Entry 5 of 91

File: USPT

May 17, 2005

US-PAT-NO: 6894639

DOCUMENT-IDENTIFIER: US 6894639 B1

TITLE: Generalized hebbian learning for principal component analysis and automatic target recognition, systems and method

DATE-ISSUED: May 17, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
<u>Katz</u> ; Alan Jerry	Dallas	TX		

US-CL-CURRENT: 342/90; 342/159, 342/175, 342/195, 342/27, 342/89, 706/15

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	KMC	Draw Desc	Ima
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☐ 6. Document ID: US 6885024 B2

L12: Entry 6 of 91

File: USPT

Apr 26, 2005

US-PAT-NO: 6885024

DOCUMENT-IDENTIFIER: US 6885024 B2

TITLE: Devices with organic crystallite active channels

DATE-ISSUED: April 26, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bao; Zhenan	Millburn	NJ		
<u>Katz</u> ; Howard Edan	Summit	NJ		
Kloc; Christian	South Orange	NJ		

US-CL-CURRENT: 257/40; 438/99

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	KMC	Draw Desc	Ima
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☐ 7. Document ID: US 6870180 B2

L12: Entry 7 of 91

File: USPT

Mar 22, 2005

US-PAT-NO: 6870180

DOCUMENT-IDENTIFIER: US 6870180 B2

TITLE: Organic polarizable gate transistor apparatus and method

DATE-ISSUED: March 22, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Dodabalapur; Ananth	Millington	NJ		
<u>Katz</u> ; Howard E.	Summit	NJ		
Sarpeshkar; Rahul	Arlington	MA		

US-CL-CURRENT: 257/40; 257/314, 257/405, 257/406, 257/410, 257/411, 257/E29.162,  
257/E29.165, 257/E29.309, 257/E51.007

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	MMIC	Draw Desc	Ima
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☐ 8. Document ID: US 6858411 B1

L12: Entry 8 of 91

File: USPT

Feb 22, 2005

US-PAT-NO: 6858411

DOCUMENT-IDENTIFIER: US 6858411 B1

**\*\* See image for Certificate of Correction \*\***

TITLE: Recombinant methods and materials for producing epothilone and epothilone derivatives

DATE-ISSUED: February 22, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Julien; Bryan	Oakland	CA		
<u>Katz</u> ; Leonard	Hayward	CA		
Khosla; Chaitan	Palo Alto	CA		
Tang; Li	Foster City	CA		
Ziermann; Rainer	San Mateo	CA		

US-CL-CURRENT: 435/76; 435/183, 435/252.31, 435/252.33, 536/23.1, 536/23.2, 536/23.7

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	MMIC	Draw Desc	Ima
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☐ 9. Document ID: US 6834294 B1

L12: Entry 9 of 91

File: USPT

Dec 21, 2004

US-PAT-NO: 6834294

DOCUMENT-IDENTIFIER: US 6834294 B1

**\*\* See image for Certificate of Correction \*\***

TITLE: Methods and systems for providing and displaying information on a keyboard

DATE-ISSUED: December 21, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
<u>Katz</u> ; Samuel F.	Givat Ze'ev			IL

US-CL-CURRENT: 709/203; 341/22, 341/23, 709/217, 709/219

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	MMIC	Draw Desc	Ima
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☐ 10. Document ID: US 6832724 B2

L12: Entry 10 of 91

File: USPT

Dec 21, 2004

US-PAT-NO: 6832724

DOCUMENT-IDENTIFIER: US 6832724 B2

TITLE: Electro-optical assembly for image projection, especially in portable instruments

DATE-ISSUED: December 21, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Yavid; Dmitriy	St. James	NY		
Wood; Frederick R.	Medford	NY		
Stern; Miklos	Flusing	NY		
Tan; Chinh	Setauket	NY		
Barkan; Edward	Miller Place	NY		
MacGregor; Shane	Forest Hills	NY		
Katz; Joseph	Stony Brook	NY		

US-CL-CURRENT: 235/454; 359/201

Full	Title	Citation	Front	Review	Classification	Date	Reference				Claims	IMC	Draw Desc	Ima
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Clear	Generate Collection	Print	Fwd Refs	Bkwd Refs	Generate OACS
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Terms	Documents
L11 and (AT or ACP or KSQ domain)	91

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Search Results - Record(s) 11 through 20 of 91 returned.

☐ 11. Document ID: US 6807223 B2

L12: Entry 11 of 91

File: USPT

Oct 19, 2004

US-PAT-NO: 6807223

DOCUMENT-IDENTIFIER: US 6807223 B2

TITLE: Method of performing code synchronization, and receiver

DATE-ISSUED: October 19, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
<u>Katz</u> ; Marcos	Oulu			FI
Glisic; Savo	Oulu			FI
Iinatti; Jari	Oulu			FI

US-CL-CURRENT: 375/149

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	ROME	Draw Desc	Ima
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☐ 12. Document ID: US 6777231 B1

L12: Entry 12 of 91

File: USPT

Aug 17, 2004

US-PAT-NO: 6777231

DOCUMENT-IDENTIFIER: US 6777231 B1

TITLE: Adipose-derived stem cells and lattices

DATE-ISSUED: August 17, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
<u>Katz</u> ; Adam J.	Charlottesville	VA		
Llull; Ramon	Mallorca			ES
Futrell; William J.	Pittsburgh	PA		
Hedrick; Marc H.	Encino	CA		
Benhaim; Prosper	Los Angeles	CA		
Lorenz; Hermann Peter	Los Angeles	CA		
Zhu; Min	Los Angeles	CA		

US-CL-CURRENT: 435/325; 435/366

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	ROME	Draw Desc	Ima
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☐ 13. Document ID: US 6771989 B1

US-PAT-NO: 6771989

DOCUMENT-IDENTIFIER: US 6771989 B1

TITLE: Method of directional radio communication

DATE-ISSUED: August 3, 2004

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Katz; Marcos	Oulu			FI
Ylitalo; Juha T	Oulu			FI

US-CL-CURRENT: 455/562.1; 455/561, 455/63.1, 455/63.4

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	FIGS	Draw Desc	Ima
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☐ 14. Document ID: US 6767536 B1

L12: Entry 14 of 91

File: USPT

Jul 27, 2004

US-PAT-NO: 6767536

DOCUMENT-IDENTIFIER: US 6767536 B1

**\*\* See image for Certificate of Correction \*\***

TITLE: Recombinant Staphylococcus thioredoxin reductase and inhibitors thereof useful as antimicrobial agents

DATE-ISSUED: July 27, 2004

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Aharonowitz; Yair	Hod Hasharon			IL
Borovok; Ilya	Ariel			IL
Cohen; Gerald	Raanana			IL
Uziel; Orit	Kfar-Saba			IL
Katz; Leonard	Oakland	CA		

US-CL-CURRENT: 424/93.42; 424/139.1, 424/165.1, 424/185.1, 424/237.1, 424/243.1,  
424/94.1, 435/191, 435/252.3, 435/36, 435/471, 435/7.33, 435/7.7, 435/91.1, 435/91.5,  
435/91.51

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	FIGS	Draw Desc	Ima
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☐ 15. Document ID: US 6765021 B2

L12: Entry 15 of 91

File: USPT

Jul 20, 2004

US-PAT-NO: 6765021

DOCUMENT-IDENTIFIER: US 6765021 B2

TITLE: 2,3,5-substituted biphenyls useful in the treatment of insulin resistance and hyperglycemia

DATE-ISSUED: July 20, 2004

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Butera; John A.	Clarkburg	NJ		
Caufield; Craig E.	New York	NY		
Graceffa; Russell F.	Hampton	NH		
Greenfield; Alexander	Princeton Junction	NJ		
Gundersen; Eric G.	Plainsboro	NJ		
Havran; Lisa Marie	Bordentown	NJ		
Katz; Alan H.	Lawrenceville	NJ		
Lennox; Joseph R.	Morrisville	NC		
Mayer; Scott C.	Robbinsville	NJ		
McDevitt; Robert E.	Somerset	NJ		

US-CL-CURRENT: 514/596; 514/476, 514/485, 514/572, 560/19, 560/43, 562/457, 564/48

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	EMC	Draw Desc	Ima

☐ 16. Document ID: US 6751597 B1

L12: Entry 16 of 91

File: USPT

Jun 15, 2004

US-PAT-NO: 6751597

DOCUMENT-IDENTIFIER: US 6751597 B1

TITLE: System and method for adaptive trade specification and match-making optimization

DATE-ISSUED: June 15, 2004

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Brodsky; Alex	Rockville	MD		
Zelivinski; Stanislav	Gaithersburg	MD		
Katz; Marcel	Rockville	MD		
Gozhansky; Alan	Rockville	MD		
Karpishpan; Sonya	Rockville	MD		

US-CL-CURRENT: 705/37; 705/35

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	EMC	Draw Desc	Ima

☐ 17. Document ID: US 6697353 B2

L12: Entry 17 of 91

File: USPT

Feb 24, 2004

US-PAT-NO: 6697353

DOCUMENT-IDENTIFIER: US 6697353 B2

TITLE: Voice-over-ATM switch architecture allowing congestion-dependent transport of silence cells

DATE-ISSUED: February 24, 2004

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bharucha; Behram H.	Millburn	NJ		

Farber; Norman	Freehold	NJ
Giuffrida; Thomas S.	Middletown	NJ
Kashper; Arik	Holmdel	NJ
Katz; Steven S.	Ocean	NJ

US-CL-CURRENT: 370/352

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	NAME	Draw Desc	Ima
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☐ 18. Document ID: US 6681132 B1

L12: Entry 18 of 91

File: USPT

Jan 20, 2004

US-PAT-NO: 6681132

DOCUMENT-IDENTIFIER: US 6681132 B1

TITLE: Sodium magnetic resonance imaging used in diagnosing tumors and assessing response to treatment

DATE-ISSUED: January 20, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Katz; Jose	Closter	NJ		
Kline; Richard Paul	Riverdale	NY		
Wu; Edward X.	New York	NY		

US-CL-CURRENT: 600/410; 324/307, 424/9.2, 436/173, 436/63, 436/64

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	NAME	Draw Desc	Ima
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☐ 19. Document ID: US 6680937 B1

L12: Entry 19 of 91

File: USPT

Jan 20, 2004

US-PAT-NO: 6680937

DOCUMENT-IDENTIFIER: US 6680937 B1

TITLE: Telecommunications network architecture for transporting fax, voice and data via an ATM switch including a STM to ATM terminal adapter

DATE-ISSUED: January 20, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bharucha; Behram H.	Millburn	NJ		
Farber; Norman	Freehold	NJ		
Giuffrida; Thomas S.	Middletown	NJ		
Kashper; Arik	Holmdel	NJ		
Katz; Steven S.	Ocean	NJ		

US-CL-CURRENT: 370/353; 370/230, 370/395.61, 370/466

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	NAME	Draw Desc	Ima
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US-PAT-NO: 6671499

DOCUMENT-IDENTIFIER: US 6671499 B1

TITLE: Method for directing antenna beam, and transceiver in a mobile communication system

DATE-ISSUED: December 30, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ylitalo; Juha	Oulu			FI
Katz; Marcos	Oulu			FI

US-CL-CURRENT: 455/101; 375/299, 455/133, 455/506, 455/562.1

Full	Title	Citation	Front	Review	Classification	Date	Reference		Claims	FIGS	Draw Desc	Imgs
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Clear	Generate Collection	Print	Fwd Refs	Bkwd Refs	Generate OACS
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Terms	Documents
L11 and (AT or ACP or KSQ domain)	91

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# Refine Search

## Search Results -

Terms	Documents
L11 and (AT or ACP or KSQ domain)	91

Database:

US Pre-Grant Publication Full-Text Database

US Patents Full-Text Database

US OCR Full-Text Database

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Search:

L12

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## Search History

DATE: Friday, March 10, 2006 [Printable Copy](#) [Create Case](#)

### Set Name Query

side by side

### Hit Count Set Name

result set

DB=USPT; PLUR=YES; OP=OR

<u>L12</u>	L11 and (AT or ACP or KSQ domain)	91	<u>L12</u>
<u>L11</u>	L7 and (KSQ domain)	91	<u>L11</u>
<u>L10</u>	L8 and (KSQ domain)	1	<u>L10</u>
<u>L9</u>	L8 and 17	1	<u>L9</u>
<u>L8</u>	revill.in.	28	<u>L8</u>
<u>L7</u>	Katz.in.	2271	<u>L7</u>
<u>L6</u>	L1 and (trixton or tween)	0	<u>L6</u>
<u>L5</u>	6627427.pn.	1	<u>L5</u>

DB=PGPB; PLUR=YES; OP=OR

<u>L4</u>	L1 and (AT specific for ethylmalonyl)	1	<u>L4</u>
<u>L3</u>	L1 and (KSQ domain)	1	<u>L3</u>
<u>L2</u>	L1 and (loading module)	1	<u>L2</u>
<u>L1</u>	20030235892	1	<u>L1</u>

END OF SEARCH HISTORY

# Refine Search

## Search Results -

Terms	Documents
6033883.pn.	1

Database:

US Pre-Grant Publication Full-Text Database

US Patents Full-Text Database

US OCR Full-Text Database

EPO Abstracts Database

JPO Abstracts Database

Derwent World Patents Index

IBM Technical Disclosure Bulletins

Search:

L6

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## Search History

DATE: Friday, March 10, 2006 [Printable Copy](#) [Create Case](#)

Set Name Query

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Hit Count Set Name

result set

*DB=USPT; PLUR=YES; OP=OR*

<u>L6</u>	6033883.pn.	1	<u>L6</u>
<u>L5</u>	6066721.pn.	1	<u>L5</u>
<u>L4</u>	5962290.pn.	1	<u>L4</u>
<u>L3</u>	6303342.pn.	1	<u>L3</u>
<u>L2</u>	5672491.pn.	1	<u>L2</u>
<u>L1</u>	6627427.pn.	1	<u>L1</u>

END OF SEARCH HISTORY

Connecting via Winsock to STN

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LOGINID:SSSPTA1653HXP

PASSWORD:

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NEWS	5	DEC 14	2006 MeSH terms loaded for MEDLINE file segment of TOXCENTER
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NEWS	7	DEC 21	IPC search and display fields enhanced in CA/Caplus with the IPC reform
NEWS	8	DEC 23	New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/USPAT2
NEWS	9	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS	10	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS	11	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS	12	JAN 17	IPC 8 in the WPI family of databases including WPIFV
NEWS	13	JAN 30	Saved answer limit increased
NEWS	14	JAN 31	Monthly current-awareness alert (SDI) frequency added to TULSA
NEWS	15	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS	16	FEB 22	Status of current WO (PCT) information on STN
NEWS	17	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS	18	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS	19	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS	20	FEB 28	MEDLINE/LMEDLINE reload improves functionality
NEWS	21	FEB 28	TOXCENTER reloaded with enhancements
NEWS	22	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS	23	MAR 01	INSPEC reloaded and enhanced
NEWS	24	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
NEWS	25	MAR 08	X.25 communication option no longer available after June 2006
NEWS EXPRESS			FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005. V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT <a href="http://download.cas.org/express/v8.0-Discover/">http://download.cas.org/express/v8.0-Discover/</a>
NEWS HOURS			STN Operating Hours Plus Help Desk Availability
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NEWS LOGIN			Welcome Banner and News Items
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TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21.

FILE 'MEDLINE' ENTERED AT 15:54:39 ON 10 MAR 2006

FILE 'USPATFULL' ENTERED AT 15:54:39 ON 10 MAR 2006

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FILE 'SCISEARCH' ENTERED AT 15:54:39 ON 10 MAR 2006

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=> s polyketide synthase gene

L1 1362 POLYKETIDE SYNTHASE GENE

=> s l1 and (encoding loading module)

L2 0 L1 AND (ENCODING LOADING MODULE)

=> s l1 and (encoding starter module)

L3 0 L1 AND (ENCODING STARTER MODULE)

=> s l1 and module

L4 237 L1 AND MODULE

=> s l4 and (AT and KSQ and ACP domains)

L5 0 L4 AND (AT AND KSQ AND ACP DOMAINS)

=> s l4 and (KSQ domain)

L6 13 L4 AND (KSQ DOMAIN)

=> s 14 and (AT specific for ethylmalonyl coA)  
L7 6 L4 AND (AT SPECIFIC FOR ETHYLMALONYL COA)

=>

=> s 14 and (ACP domain)  
L8 75 L4 AND (ACP DOMAIN)

=> s 18 and 17 and 16  
L9 1 L8 AND L7 AND L6

=> d 19 ti abs ibib tot

L9 ANSWER 1 OF 1 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN  
TI Novel recombinant host cell (*Saccharopolyspora erythraea*) comprising  
recombinant biosynthetic pathways for producing precursor (butyryl CoA)  
required for biosynthesis of a product (propyl-6-deoxyerythronolide B);  
recombinant bacterium useful for antibiotic production  
AN 2002-11559 BIOTECHDS  
AB DERWENT ABSTRACT:  
NOVELTY - A recombinant host cell (I) having one or more expression  
vectors expressing enzymes (II) capable of making product (P) and  
precursor (PR) required for biosynthesis of (P) in (I), where (I): (a) is  
unable to make (P) due to lack of all/part of a biosynthetic pathway  
required to produce PR; or (b) makes (P) in much smaller amounts due to  
PR being present in low amounts in the absence of (II), is new.  
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the  
following: (1) a recombinant **polyketide synthase**  
**gene** (III) that encodes a loading **module** comprising a  
ketosynthase (KS)Q domain, an acyl transferase (AT) **specific**  
for **ethylmalonyl CoA**, and an acyl carrier protein (**ACP**) **domain**; and (2) a host cell (IV) that comprises  
(III), and a recombinant gene such as recombinant *ccr* or *icm* genes.  
WIDER DISCLOSURE - The following are disclosed: (1) a hybrid  
polyketide synthase (PKS) in which the loading **module** is  
composed of **KSQ domain**, an ethylmalonyl CoA specific  
AT domain, and an **ACP domain**, and AT domain specific  
for malonyl CoA; (2) recombinant DNA expression vectors and methods for  
making a polyketide and its required precursors in any host cell; (3)  
methods and genetic constructs for producing a glycosylated and/or  
hydroxylated polyketide compounds directly in the host cell of interest;  
(4) modified polyketide products of PKS which are further modified by  
hydroxylation and glycosylation reaction to exhibit antibiotic activity;  
and (5) novel ketolide compounds, polyketide compounds with potent  
antibiotic activity of significant interest due to activity against  
antibiotic resistant strain of bacteria.  
BIOTECHNOLOGY - Preferred Host Cell: PR is preferably a primary  
metabolite that is produced in a first cell but not in a second  
heterologous cell. (I) comprises one or more expression vectors that  
drive expression of enzymes capable of making a product (polyketide,  
preferably propyl-6-deoxyerythronolide B (6-dEB) synthesized by modular  
polyketide synthase (PKS)) and a precursor (butyryl CoA) required for the  
biosynthesis of the product in the cell. Optionally, (I) is a *eryM* mutant  
producing a polyketide. Additionally, (I) comprises: (a) recombinant *ccr*,  
*acsA*, *bdh*, and *ech* genes; (b) recombinant *icm*, *vdh*, *ccr*, *acsA*, *vdh*, and  
*ech* genes; or (c) recombinant *icm*, *ccr*, *acsA*, *bdh*, and *ech* genes.  
Preferably propyl-6-dEB is produced by a modular PKS in a host cell  
comprising mutation in *eryM* gene, involving a precursor biosynthetic  
enzyme such as propionyl CoA decarboxylase that converts propionyl CoA to  
methyl melanoyl CoA. The cell is preferably further modified to  
overexpress a biotin transferase enzyme encoded by the *birA* gene. (I) is  
optionally a *Streptomyces fradiae* cell expressing one or more genes  
encoding an erythromycin biosynthetic enzyme, and is producing

15-methylerythromycin.

ACTIVITY - Antimicrobial.

MECHANISM OF ACTION - Antibiotic. No suitable data given.

USE - (I) (*Saccharopolyspora erythraea* cell which does not express a functional *eryM* gene product) is useful for producing 14,15-propenylerythromycin and/or the corresponding 14,15-propenyl-6-deoxyerythronolide B. The method involves culturing (I) that expresses isobutyryl CoA mutase, valine dehydrogenase, butyryl CoA dehydrogenase, and 6-deoxyerythronolide polyketide synthase. The butyryl CoA dehydrogenase is expressed from gene isolated from *Clostridium acetobutylicum* or *Mycobacterium tuberculosis* (*fadE25*) (claimed). (I) is useful for producing polyketides (both macrolide aglycones and their modified derivatives) that are naturally occurring or produced by recombinant DNA technology. The polyketides produced are useful intermediates in formation of compounds with antibiotic or other activity through hydroxylation, epoxidation, and glycosylation reactions. The polyketides are useful as antibiotics and as intermediates in synthesis of other useful compounds such as erythromycin. The erythromycin analogs produced using (I) are used clinically as prokinetic agents to induce phase III of migrating motor complexes, to increase esophageal peristalsis, etc.

ADMINISTRATION - The polyketide compounds are administered orally, topically, parenterally or by inhalation spray. Dosages of the compound range from 0.01-50 (preferably 0.1-10) mg/kg body weight/day.

EXAMPLE - Construction of *eryM* knockout strains and production of 15-methyl-erythromycin was carried out follows. The construction of two recombinant DNA vectors designed to disrupt the *eryM* gene in *Saccharopolyspora erythraea* by single crossover was performed by the following method. These vectors can be used to generate a strain of *S.erythraea* that produces higher titers of 15-methyl erythromycin A or C than does wild-type *S.erythraea* under the same conditions without the need for the addition of an exogenous diketide. The desired strain differed from the wild-type strain in that intracellular pools of propanoyl-CoA were greatly reduced, pools of butanoyl-CoA were greatly elevated, and pools of methylmalonyl-CoA remain high. Disruption of the *eryM* gene, which encoded methylmalonyl decarboxylase, caused loss of erythromycin production that can be restored by feeding propionate, methylpropionate, or propanol in a wild-type strain of *S.erythraea*. The *S.erythraea* *eryM* gene was isolated by PCR or the coding region. An internal fragment of the *eryM* gene was isolated by polymerase chain reaction (PCR) and cloned into the *Xba*I and *Hind*III sites of the vectors pWHM3 (a *Streptomyces* vector) (conferred thiostrepton resistance) and pOJ260 (a *Streptomyces* vector) (conferred apramycin resistance) or gene disruption. The resulting vectors were propagated in *Escherichia coli* ET12567 to obtain unmethylated DNA. The above constructs were then introduced into a high-producing *S.erythraea* strain for gene disruption by homologous recombination. Protoplast transformation of this strain was very difficult, transformants were only obtained only using alkali-denatured, non-methylated DNA of only the pOJ260-derived construct. The transformant strains were grown for DNA isolation and in a standard two-stage shake flask fermentation procedure to evaluate production. Metabolites were quantitated by ion counting in a mass spectrometer relative to a roxithromycin internal standard. Putative *eryM* knockout transformants were shown to be correct by Southern blot hybridization. The mutant displayed the same morphology as the parent strain, both in liquid medium and on agar plates. The parent strain and two isolates of the *eryM*- mutant were grown using the shake flask procedure. In addition to the oil plus propanol feed, culture flasks were fed equivalent levels of oil alone, oil plus butanol, oil plus propionate, and oil plus butyrate. The cultures were killed by the propionate and butyrate feeds, and these flasks were discarded. Samples were taken from other flasks each day and the set was analyzed by ion counting. Production of erythromycin A and B by the *eryM*- mutant was

similar to that of the corresponding wild-type strain when fed oil alone or oil and propanol in rich medium. For both strains, production of erythromycin A and B was depressed with an oil and butanol feed. While knockout of eryM did not reduce production of erythromycin A and B in rich medium in the dramatic way. The high-producing wild-type strain appeared to produce low levels of 15-methyl-erythromycins when butanol was fed instead of propanol. The eryM- mutant produced a higher maximum percentage 15-methyl-erythromycin A and B with an oil and butanol feed compared to the wild-type strain, demonstrating that propionyl CoA levels were reduced in the eryM- strain. (85 pages)

ACCESSION NUMBER: 2002-11559 BIOTECHDS

TITLE: Novel recombinant host cell (*Saccharopolyspora erythraea*) comprising recombinant biosynthetic pathways for producing precursor (butyryl CoA) required for biosynthesis of a product (propyl-6-deoxyerythronolide B); recombinant bacterium useful for antibiotic production

AUTHOR: KATZ L; REVILL P

PATENT ASSIGNEE: KOSAN BIOSCIENCES INC

PATENT INFO: WO 2001031049 3 May 2001

APPLICATION INFO: WO 1999-US29447 25 Oct 1999

PRIORITY INFO: US 1999-161414 25 Oct 1999

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-256023 [30]

=> d his

(FILE 'HOME' ENTERED AT 15:53:58 ON 10 MAR 2006)

FILE 'MEDLINE, USPATFULL, DGENE, EMBASE, WPIDS, FSTA, JICST-EPLUS, BIOSIS, BIOTECHDS, SCISEARCH' ENTERED AT 15:54:39 ON 10 MAR 2006

```
L1      1362 S POLYKETIDE SYNTHASE GENE
L2      0 S L1 AND (ENCODING LOADING MODULE)
L3      0 S L1 AND (ENCODING STARTER MODULE)
L4      237 S L1 AND MODULE
L5      0 S L4 AND (AT AND KSQ AND ACP DOMAINS)
L6      13 S L4 AND (KSQ DOMAIN)
L7      6 S L4 AND (AT SPECIFIC FOR ETHYLMALONYL COA)
L8      75 S L4 AND (ACP DOMAIN)
L9      1 S L8 AND L7 AND L6
```

=> e katz, l/au

```
E1      3      KATZ ZEILIG M/AU
E2      14     KATZ ZVI/AU
E3      0 --> KATZ, L/AU
E4      1      KATZAGIANNAKIS J/AU
E5      1      KATZAKIAN/AU
E6      7      KATZAKIAN A/AU
E7      1      KATZAKIAN A J/AU
E8      2      KATZAKIAN ARTHUR/AU
E9      1      KATZAKIAN JOHN/AU
E10     17     KATZAKIAN JR ARTHUR/AU
E11     1      KATZAKIAN TERRY A/AU
E12     3      KATZAMAN R E/AU
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=> e revill, p/au

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E1      25     REVILL W PETER/AU
E2      2      REVILL WP/AU
E3      0 --> REVILL, P/AU
E4      33     REVILLA A/AU
E5      1      REVILLA A D/AU
E6      1      REVILLA A G/AU
```

E7 1 REVILLA A G JR/AU  
 E8 21 REVILLA A L/AU  
 E9 10 REVILLA A P/AU  
 E10 1 REVILLA A P DE/AU  
 E11 1 REVILLA A V JR/AU  
 E12 2 REVILLA A Z/AU

=> d his

(FILE 'HOME' ENTERED AT 15:53:58 ON 10 MAR 2006)

FILE 'MEDLINE, USPATFULL, DGENE, EMBASE, WPIDS, FSTA, JICST-EPLUS, BIOSIS, BIOTECHDS, SCISEARCH' ENTERED AT 15:54:39 ON 10 MAR 2006

L1 1362 S POLYKETIDE SYNTHASE GENE  
 L2 0 S L1 AND (ENCODING LOADING MODULE)  
 L3 0 S L1 AND (ENCODING STARTER MODULE)  
 L4 237 S L1 AND MODULE  
 L5 0 S L4 AND (AT AND KSQ AND ACP DOMAINS)  
 L6 13 S L4 AND (KSQ DOMAIN)  
 L7 6 S L4 AND (AT SPECIFIC FOR ETHYLMALONYL COA)  
 L8 75 S L4 AND (ACP DOMAIN)  
 L9 1 S L8 AND L7 AND L6  
 E KATZ, L/AU  
 E REVILL, P/AU

=> d l7 ti abs ibib tot

L7 ANSWER 1 OF 6 USPATFULL on STN  
 TI Production of polyketides  
 AB Recombinant host cells that comprise recombinant DNA expression vectors that drive expression of a product and a precursor for biosynthesis of that product can be used to produce useful products such as polyketides in host cells that do not naturally produce the product or produce the product at low levels due to the absence of the precursor or the presence of the precursor in rate limiting amounts.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2003:335016 USPATFULL  
 TITLE: Production of polyketides  
 INVENTOR(S): Katz, Leonard, Oakland, CA, UNITED STATES  
 Revill, Peter, Oakland, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003235892	A1	20031225
APPLICATION INFO.:	US 2003-607809	A1	20030627 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 2000-697022, filed on 25 Oct 2000, GRANTED, Pat. No. US 6627427		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-161414P	19991025 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	MORRISON & FOERSTER LLP, 3811 VALLEY CENTRE DRIVE, SUITE 500, SAN DIEGO, CA, 92130-2332	

NUMBER OF CLAIMS: 6  
 EXEMPLARY CLAIM: 1  
 NUMBER OF DRAWINGS: 2 Drawing Page(s)  
 LINE COUNT: 2751  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 2 OF 6 USPATFULL on STN

TI Polynucleotides encoding the fkbA gene of the FK-520 **polyketide synthase gene** cluster  
AB Host cells comprising recombinant vectors encoding the FK-520 polyketide synthase and FK-520 modification enzymes can be used to produce the FK-520 polyketide. Recombinant DNA constructs comprising one or more FK-520 polyketide synthase domains, modules, open reading frames, and variants thereof can be used to produce recombinant polyketide synthases and a variety of different polyketides with application as pharmaceutical and veterinary products.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2003:251115 USPATFULL  
TITLE: Polynucleotides encoding the fkbA gene of the FK-520 **polyketide synthase gene** cluster  
INVENTOR(S): Reeves, Christopher, Orinda, CA, UNITED STATES  
Chu, Daniel, Santa Clara, CA, UNITED STATES  
Khosla, Chaitan, Palo Alto, CA, UNITED STATES  
Santi, Daniel, San Francisco, CA, UNITED STATES  
Wu, Kai, Foster City, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003175901	A1	20030918
	US 6759536	B2	20040706
APPLICATION INFO.:	US 2001-940316	A1	20010827 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 1999-410551, filed on 1 Oct 1999, GRANTED, Pat. No. US 6503737		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-102748P	19981002 (60)
	US 1999-123810P	19990311 (60)
	US 1999-139650P	19990617 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	MORRISON & FOERSTER LLP, 3811 VALLEY CENTRE DRIVE, SUITE 500, SAN DIEGO, CA, 92130-2332	
NUMBER OF CLAIMS:	20	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	9 Drawing Page(s)	
LINE COUNT:	13940	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 3 OF 6 USPATFULL on STN

TI Isolated nucleic acids relating to the fkbA gene within the FK-520 **polyketide synthase gene** cluster  
AB Host cells comprising recombinant vectors encoding the FK-520 polyketide synthase and FK-520 modification enzymes can be used to produce the FK-520 polyketide. Recombinant DNA constructs comprising one or more FK-520 polyketide synthase domains, modules, open reading frames, and variants thereof can be used to produce recombinant polyketide synthases and a variety of different polyketides with application as pharmaceutical and veterinary products.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2003:6812 USPATFULL  
TITLE: Isolated nucleic acids relating to the fkbA gene within the FK-520 **polyketide synthase gene** cluster  
INVENTOR(S): Reeves, Christopher, Orinda, CA, United States  
Chu, Daniel, Santa Clara, CA, United States  
Khosla, Chaitan, Palo Alto, CA, United States

PATENT ASSIGNEE(S): Santi, Daniel, San Francisco, CA, United States  
Wu, Kai, Foster City, CA, United States  
Kosan Biosciences, Inc., Hayward, CA, United States  
(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6503737	B1	20030107
APPLICATION INFO.:	US 1999-410551		19991001 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-102748P	19981002 (60)
	US 1999-139650P	19990617 (60)
	US 1999-123810P	19990311 (60)

DOCUMENT TYPE: Utility  
FILE SEGMENT: GRANTED  
PRIMARY EXAMINER: Achutamurthy, Ponnathapura  
ASSISTANT EXAMINER: Kerr, Kathleen M  
LEGAL REPRESENTATIVE: Wllach, Brenda J., Ring, Christine, Kaster, Kevin  
NUMBER OF CLAIMS: 34  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 8 Drawing Figure(s); 9 Drawing Page(s)  
LINE COUNT: 13428  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 4 OF 6 USPATFULL on STN

TI Polyketide synthase enzymes and recombinant DNA constructs therefor  
AB Host cells comprising recombinant vectors encoding the FK-520 polyketide synthase and FK-520 modification enzymes can be used to produce the FK-520 polyketide. Recombinant DNA constructs comprising one or more FK-520 polyketide synthase domains, modules, open reading frames, and variants thereof can be used to produce recombinant polyketide synthases and a variety of different polyketides with application as pharmaceutical and veterinary products.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:17448 USPATFULL  
TITLE: Polyketide synthase enzymes and recombinant DNA constructs therefor  
INVENTOR(S): Reeves, Christopher, Orinda, CA, UNITED STATES  
Chu, Daniel, Santa Clara, CA, UNITED STATES  
Khosla, Chaitan, Palo Alto, CA, UNITED STATES  
Santi, Daniel, San Francisco, CA, UNITED STATES  
Wu, Kai, Foster City, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002010328	A1	20020124
	US 6660862	B2	20031209
APPLICATION INFO.:	US 2001-825621	A1	20010403 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 1999-410551, filed on 1 Oct 1999, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	WO 1999-US22886	19991001
	US 1998-102748P	19981002 (60)
	US 1999-123810P	19990311 (60)
	US 1999-139650P	19990617 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Carolyn A. Favorito, Morrison & Foerster LLP, Suite	

500, 3811 Valley Centre Drive, San Diego, CA,  
92130-2332

NUMBER OF CLAIMS: 20  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 9 Drawing Page(s)  
LINE COUNT: 4752  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 5 OF 6 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN  
TI Novel recombinant host cell (*Saccharopolyspora erythraea*) comprising recombinant biosynthetic pathways for producing precursor (butyryl CoA) required for biosynthesis of a product (propyl-6-deoxyerythronolide B).  
AN 2002-256023 [30] WPIDS  
CR 2001-308652 [32]  
AB WO 200131049 A UPAB: 20040202  
NOVELTY - A recombinant host cell (I) having one or more expression vectors expressing enzymes (II) capable of making product (P) and precursor (PR) required for biosynthesis of (P) in (I), where (I):  
(a) is unable to make (P) due to lack of all/part of a biosynthetic pathway required to produce PR; or  
(b) makes (P) in much smaller amounts due to PR being present in low amounts in the absence of (II), is new.  
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:  
(1) a recombinant **polyketide synthase gene** (III) that encodes a loading **module** comprising a ketosynthase (KS)Q domain, an acyl transferase (AT) **specific for ethylmalonyl CoA**, and an acyl carrier protein (ACP) domain; and  
(2) a host cell (IV) that comprises (III), and a recombinant gene such as recombinant ccr or icm genes.  
ACTIVITY - Antimicrobial.  
MECHANISM OF ACTION - Antibiotic.  
No suitable data given.  
USE - (I) (*Saccharopolyspora erythraea* cell which does not express a functional eryM gene product) is useful for producing 14,15-propenylerythromycin and/or the corresponding 14,15-propenyl-6-deoxyerythronolide B. The method involves culturing (I) that expresses isobutyryl CoA mutase, valine dehydrogenase, butyryl CoA dehydrogenase, and 6-deoxyerythronolide polyketide synthase. The butyryl CoA dehydrogenase is expressed from gene isolated from *Clostridium acetobutylicum* or *Mycobacterium tuberculosis* (fadE25) (claimed).  
(I) is useful for producing polyketides (both macrolide aglycones and their modified derivatives) that are naturally occurring or produced by recombinant DNA technology. The polyketides produced are useful intermediates in formation of compounds with antibiotic or other activity through hydroxylation, epoxidation, and glycosylation reactions. The polyketides are useful as antibiotics and as intermediates in synthesis of other useful compounds such as erythromycin. The erythromycin analogs produced using (I) are used clinically as prokinetic agents to induce phase III of migrating motor complexes, to increase esophageal peristalsis, etc.

Dwg.0/2

ACCESSION NUMBER: 2002-256023 [30] WPIDS  
CROSS REFERENCE: 2001-308652 [32]  
DOC. NO. CPI: C2002-076316  
TITLE: Novel recombinant host cell (*Saccharopolyspora erythraea*) comprising recombinant biosynthetic pathways for producing precursor (butyryl CoA) required for biosynthesis of a product (propyl-6-deoxyerythronolide B).  
DERWENT CLASS: B03 B04 B05 C06 D16  
INVENTOR(S): KATZ, L; REVILL, P; DAYEM, L; KEALEY, J; SANTI, D

PATENT ASSIGNEE(S): (KOSA-N) KOSAN BIOSCIENCES INC; (DAYE-I) DAYEM L;  
 (KEAL-I) KEALEY J; (SANT-I) SANTI D; (KATZ-I) KATZ L;  
 (REVI-I) REVILL P  
 COUNTRY COUNT: 95  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001031049	A2	20010503	(200230)*	EN	85
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
AU 2001012317	A	20010508	(200230)		
EP 1224317	A2	20020724	(200256)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
US 2002142401	A1	20021003	(200267)		
US 6627427	B1	20030930	(200367)		
US 2003235892	A1	20031225	(200408)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001031049	A2	WO 2000-US29447	20001025
AU 2001012317	A	AU 2001-12317	20001025
EP 1224317	A2	EP 2000-973861	20001025
		WO 2000-US29447	20001025
US 2002142401	A1 Provisional	US 1999-161414P	19991025
	Provisional	US 1999-161703P	19991027
	Provisional	US 2000-206082P	20000518
	Div ex	US 2000-699136	20001027
		US 2001-942407	20010829
US 6627427	B1 Provisional	US 1999-161414P	19991025
		US 2000-697022	20001025
US 2003235892	A1 Provisional	US 1999-161414P	19991025
	Div ex	US 2000-697022	20001025
		US 2003-607809	20030627

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001012317	A Based on	WO 2001031049
EP 1224317	A2 Based on	WO 2001031049
US 2003235892	A1 Div ex	US 6627427

PRIORITY APPLN. INFO: US 1999-161414P 19991025; US  
 1999-161703P 19991027; US  
 2000-206082P 20000518; US  
 2000-699136 20001027; US  
 2001-942407 20010829; US  
 2000-697022 20001025; US  
 2003-607809 20030627

L7 ANSWER 6 OF 6 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN.  
 TI Novel recombinant host cell (Saccharopolyspora erythraea) comprising  
 recombinant biosynthetic pathways for producing precursor (butyryl CoA)  
 required for biosynthesis of a product (propyl-6-deoxyerythronolide B);  
 recombinant bacterium useful for antibiotic production

AN 2002-11559 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - A recombinant host cell (I) having one or more expression vectors expressing enzymes (II) capable of making product (P) and precursor (PR) required for biosynthesis of (P) in (I), where (I): (a) is unable to make (P) due to lack of all/part of a biosynthetic pathway required to produce PR; or (b) makes (P) in much smaller amounts due to PR being present in low amounts in the absence of (II), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a recombinant **polyketide synthase gene** (III) that encodes a loading **module** comprising a ketosynthase (KS)Q domain, an acyl transferase (AT) **specific** for **ethylmalonyl CoA**, and an acyl carrier protein (ACP) domain; and (2) a host cell (IV) that comprises (III), and a recombinant gene such as recombinant ccr or icm genes.

WIDER DISCLOSURE - The following are disclosed: (1) a hybrid polyketide synthase (PKS) in which the loading **module** is composed of KSQ domain, an ethylmalonyl CoA specific AT domain, and an ACP domain, and AT domain specific for malonyl CoA; (2) recombinant DNA expression vectors and methods for making a polyketide and its required precursors in any host cell; (3) methods and genetic constructs for producing a glycosylated and/or hydroxylated polyketide compounds directly in the host cell of interest; (4) modified polyketide products of PKS which are further modified by hydroxylation and glycosylation reaction to exhibit antibiotic activity; and (5) novel ketolide compounds, polyketide compounds with potent antibiotic activity of significant interest due to activity against antibiotic resistant strain of bacteria.

BIOTECHNOLOGY - Preferred Host Cell: PR is preferably a primary metabolite that is produced in a first cell but not in a second heterologous cell. (I) comprises one or more expression vectors that drive expression of enzymes capable of making a product (polyketide, preferably propyl-6-deoxyerythronolide B (6-dEB) synthesized by modular polyketide synthase (PKS)) and a precursor (butyryl CoA) required for the biosynthesis of the product in the cell. Optionally, (I) is a eryM mutant producing a polyketide. Additionally, (I) comprises: (a) recombinant ccr, acsA, bdh, and ech genes; (b) recombinant icm, vdh, ccr, acsA, vdh, and ech genes; or (c) recombinant icm, ccr, acsA, bdh, and ech genes. Preferably propyl-6-dEB is produced by a modular PKS in a host cell comprising mutation in eryM gene, involving a precursor biosynthetic enzyme such as propionyl CoA decarboxylase that converts propionyl CoA to methyl melanoyl CoA. The cell is preferably further modified to overexpress a biotin transferase enzyme encoded by the birA gene. (I) is optionally a Streptomyces fradiae cell expressing one or more genes encoding an erythromycin biosynthetic enzyme, and is producing 15-methylerythromycin.

ACTIVITY - Antimicrobial.

MECHANISM OF ACTION - Antibiotic. No suitable data given.

USE - (I) (Saccharopolyspora erythraea cell which does not express a functional eryM gene product) is useful for producing 14,15-propenylerythromycin and/or the corresponding 14,15-propenyl-6-deoxyerythronolide B. The method involves culturing (I) that expresses isobutyryl CoA mutase, valine dehydrogenase, butyryl CoA dehydrogenase, and 6-deoxyerythronolide polyketide synthase. The butyryl CoA dehydrogenase is expressed from gene isolated from Clostridium acetobutylicum or Mycobacterium tuberculosis (fadE25) (claimed). (I) is useful for producing polyketides (both macrolide aglycones and their modified derivatives) that are naturally occurring or produced by recombinant DNA technology. The polyketides produced are useful intermediates in formation of compounds with antibiotic or other activity through hydroxylation, epoxidation, and glycosylation reactions. The polyketides are useful as antibiotics and as intermediates in synthesis of other useful compounds such as erythromycin. The erythromycin analogs

produced using (I) are used clinically as prokinetic agents to induce phase III of migrating motor complexes, to increase esophageal peristalsis, etc.

ADMINISTRATION - The polyketide compounds are administered orally, topically, parenterally or by inhalation spray. Dosages of the compound range from 0.01-50 (preferably 0.1-10) mg/kg body weight/day.

EXAMPLE - Construction of eryM knockout strains and production of 15-methyl-erythromycin was carried out follows. The construction of two recombinant DNA vectors designed to disrupt the eryM gene in *Saccharopolyspora erythraea* by single crossover was performed by the following method. These vectors can be used to generate a strain of *S.erythraea* that produces higher titers of 15-methyl erythromycin A or C than does wild-type *S.erythraea* under the same conditions without the need for the addition of an exogenous diketide. The desired strain differed from the wild-type strain in that intracellular pools of propanoyl-CoA were greatly reduced, pools of butanoyl-CoA were greatly elevated, and pools of methylmalonyl-CoA remain high. Disruption of the eryM gene, which encoded methylmalonyl decarboxylase, caused loss of erythromycin production that can be restored by feeding propionate, methylpropionate, or propanol in a wild-type strain of *S.erythraea*. The *S.erythraea* eryM gene was isolated by PCR or the coding region. An internal fragment of the eryM gene was isolated by polymerase chain reaction (PCR) and cloned into the XbaI and HindIII sites of the vectors pWHM3 (a *Streptomyces* vector) (conferred thiostrepton resistance) and pOJ260 (a *Streptomyces* vector) (conferred apramycin resistance) or gene disruption. The resulting vectors were propagated in *Escherichia coli* ET12567 to obtain unmethylated DNA. The above constructs were then introduced into a high-producing *S.erythraea* strain for gene disruption by homologous recombination. Protoplast transformation of this strain was very difficult, transformants were only obtained only using alkali-denatured, non-methylated DNA of only the pOJ260-derived construct. The transformant strains were grown for DNA isolation and in a standard two-stage shake flask fermentation procedure to evaluate production. Metabolites were quantitated by ion counting in a mass spectrometer relative to a roxithromycin internal standard. Putative eryM knockout transformants were shown to be correct by Southern blot hybridization. The mutant displayed the same morphology as the parent strain, both in liquid medium and on agar plates. The parent strain and two isolates of the eryM- mutant were grown using the shake flask procedure. In addition to the oil plus propanol feed, culture flasks were fed equivalent levels of oil alone, oil plus butanol, oil plus propionate, and oil plus butyrate. The cultures were killed by the propionate and butyrate feeds, and these flasks were discarded. Samples were taken from other flasks each day and the set was analyzed by ion counting. Production of erythromycin A and B by the eryM- mutant was similar to that of the corresponding wild-type strain when fed oil alone or oil and propanol in rich medium. For both strains, production of erythromycin A and B was depressed with an oil and butanol feed. While knockout of eryM did not reduce production of erythromycin A and B in rich medium in the dramatic way. The high-producing wild-type strain appeared to produce low levels of 15-methyl-erythromycins when butanol was fed instead of propanol. The eryM- mutant produced a higher maximum percentage 15-methyl-erythromycin A and B with an oil and butanol feed compared to the wild-type strain, demonstrating that propionyl CoA levels were reduced in the eryM- strain. (85 pages)

ACCESSION NUMBER: 2002-11559 BIOTECHDS

TITLE: Novel recombinant host cell (*Saccharopolyspora erythraea*) comprising recombinant biosynthetic pathways for producing precursor (butyryl CoA) required for biosynthesis of a product (propyl-6-deoxyerythronolide B);  
recombinant bacterium useful for antibiotic production

AUTHOR: KATZ L; REVILL P

PATENT ASSIGNEE: KOSAN BIOSCIENCES INC

PATENT INFO: WO 2001031049 3 May 2001  
APPLICATION INFO: WO 1999-US29447 25 Oct 1999  
PRIORITY INFO: US 1999-161414 25 Oct 1999  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2002-256023 [30]

=> d his

(FILE 'HOME' ENTERED AT 15:53:58 ON 10 MAR 2006)

FILE 'MEDLINE, USPATFULL, DGENE, EMBASE, WPIDS, FSTA, JICST-EPLUS;  
BIOSIS, BIOTECHDS, SCISEARCH' ENTERED AT 15:54:39 ON 10 MAR 2006

L1 1362 S POLYKETIDE SYNTHASE GENE  
L2 0 S L1 AND (ENCODING LOADING MODULE)  
L3 0 S L1 AND (ENCODING STARTER MODULE)  
L4 237 S L1 AND MODULE  
L5 0 S L4 AND (AT AND KSQ AND ACP DOMAINS)  
L6 13 S L4 AND (KSQ DOMAIN)  
L7 6 S L4 AND (AT SPECIFIC FOR ETHYLMALONYL COA)  
L8 75 S L4 AND (ACP DOMAIN)  
L9 1 S L8 AND L7 AND L6  
E KATZ, L/AU  
E REVILL, P/AU

=> s 16 and 18

L10 7 L6 AND L8

=> d l10 ti abs ibib tot

L10 ANSWER 1 OF 7 USPATFULL on STN  
TI Recombinant narbonolide polyketide synthase  
AB Recombinant DNA compounds that encode all or a portion of the  
narbonolide polyketide synthase are used to express recombinant  
polyketide synthase genes in host cells for the production of  
narbonolide, narbonolide derivatives, and polyketides that are useful as  
antibiotics and as intermediates in the synthesis of compounds with  
pharmaceutical value.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2005:30813 USPATFULL  
TITLE: Recombinant narbonolide polyketide synthase  
INVENTOR(S): Ashley, Gary, Alameda, CA, UNITED STATES  
Betlach, Melanie C., San Francisco, CA, UNITED STATES  
Betlach, Mary, San Francisco, CA, UNITED STATES  
McDaniel, Robert, Palo Alto, CA, UNITED STATES  
Tang, Li, Foster City, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005026244	A1	20050203
APPLICATION INFO.:	US 2004-468828	A1	20040415 (10)
	WO 2002-US5642		20020222
RELATED APPLN. INFO.:	Continuation of Ser. No. US 2001-793708, filed on 22 Feb 2001, PENDING Continuation-in-part of Ser. No. US 2000-657440, filed on 7 Sep 2000, GRANTED, Pat. No. US 6509455 Division of Ser. No. US 1999-320878, filed on 27 May 1999, GRANTED, Pat. No. US 6117659 Continuation-in-part of Ser. No. US 1998-141908, filed on 28 Aug 1998, GRANTED, Pat. No. US 6503741 Continuation-in-part of Ser. No. US 1998-73538, filed on 6 May 1998, GRANTED, Pat. No. US 6558942		

Continuation-in-part of Ser. No. US 1997-846247, filed  
on 30 Apr 1997, GRANTED, Pat. No. US 6391594

DOCUMENT TYPE: Utility  
FILE SEGMENT: APPLICATION  
LEGAL REPRESENTATIVE: MORRISON & FOERSTER LLP, 755 PAGE MILL RD, PALO ALTO,  
CA, 94304-1018  
NUMBER OF CLAIMS: 20  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 6 Drawing Page(s)  
LINE COUNT: 7804  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 2 OF 7 USPATFULL on STN

TI Polyketides and their synthesis  
AB The complete sequence of the gene cluster for the monensin type I  
polyketide synthase, from *S. cinnamomensis*, is provided. Thus variant  
polyketides containing monensin-derived elements can be genetically  
engineered. Furthermore there are novel features, e.g. a regulatory  
protein mon RI, which are of wide utility.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2004:280345 USPATFULL  
TITLE: Polyketides and their synthesis  
INVENTOR(S): Leadley, Peter Francis, Cambridge, UNITED KINGDOM  
Staunton, James, Cambridge, UNITED KINGDOM  
Oliynyk, Mark Yan, Cambridge, UNITED KINGDOM

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004219645	A1	20041104
APPLICATION INFO.:	US 2002-980217	A1	20020506 (9)
	WO 2001-GB2072		20010530

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1999-12563	19990528
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	DANN, DORFMAN, HERRELL & SKILLMAN, saet, 1601 MARKET STREET, PHILADELPHIA, PA, 19103-2307	
NUMBER OF CLAIMS:	45	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	4 Drawing Page(s)	
LINE COUNT:	8550	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 3 OF 7 USPATFULL on STN

TI Hybrid glycosylated products and their production and use  
AB The present invention relates to hybrid glycosylated products, and in  
particular, to natural products such as polyketides and glycopeptides,  
and to processes for their preparation. The invention is particularly  
concerned with recombinant cells in which a cloned microbial  
glycosyltransferase can be conveniently screened for its ability to  
generate specific glycosylated derivatives when supplied with  
polyketide, peptide, or polyketide-peptides as substrates. The invention  
demonstrates that cloned glycosyltransferases when rapidly screened for  
their ability to attach a range of activated sugars to a range of  
exogenously supplied or endogenously generated aglycone templates, show  
a surprising flexibility towards both aglycone and sugar substrates, and  
that this process allows the production of glycosylated polyketides in  
good yield. This overcomes the problem not only of supplying novel sugar  
attachments to individual polyketides, including polyketides altered by  
genetic engineering, but also of increasing the diversity of polyketide

libraries by combinatorial attachment of sugars.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2003:288667 USPATFULL  
TITLE: Hybrid glycosylated products and their production and use  
INVENTOR(S): Leadlay, Peter Francis, Gaupe Rd Cambridge, UNITED KINGDOM  
Staunton, James, Cambridge, UNITED KINGDOM  
Gaisser, Sabine, Cambridge, UNITED KINGDOM

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003203425	A1	20031030
APPLICATION INFO.:	US 2003-257549	A1	20030325 (10)
	WO 2001-GB1743		20010417

	NUMBER	DATE
PRIORITY INFORMATION:	GB 2000-9207	20000413
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	DANN, DORFMAN, HERRELL & SKILLMAN, 1601 MARKET STREET, SUITE 2400, PHILADELPHIA, PA, 19103-2307	
NUMBER OF CLAIMS:	57	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	40 Drawing Page(s)	
LINE COUNT:	2503	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 4 OF 7 USPATFULL on STN

TI Heterologous production of 15-methyl-6-deoxyerthronolide B  
AB Recombinant host cells that comprise recombinant DNA expression vectors that drive expression of a product and a precursor for biosynthesis of that product can be used to produce useful products such as polyketides in host cells that do not naturally produce the product or produce the product at low levels due to the absence of the precursor or the presence of the precursor in rate limiting amounts.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2003:260669 USPATFULL  
TITLE: Heterologous production of 15-methyl-6-deoxyerthronolide B  
INVENTOR(S): Katz, Leonard, Oakland, CA, United States  
Revill, Peter, Oakland, CA, United States  
PATENT ASSIGNEE(S): Kosan Biosciences, Inc., Hayward, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6627427	B1	20030930
APPLICATION INFO.:	US 2000-697022		20001025 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-161414P	19991025 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Achutamurthy, Ponnathapu	
ASSISTANT EXAMINER:	Kerr, Kathleen	
LEGAL REPRESENTATIVE:	Morrison & Foerster LLP, Kaster, Kevin	
NUMBER OF CLAIMS:	12	
EXEMPLARY CLAIM:	1	

NUMBER OF DRAWINGS: 20 Drawing Figure(s); 20 Drawing Page(s)  
LINE COUNT: 3167  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 5 OF 7 USPATFULL on STN

TI Recombinant narbonolide polyketide synthase  
AB Recombinant DNA compounds that encode all or a portion of the narbonolide polyketide synthase are used to express recombinant polyketide synthase genes in host cells for the production of narbonolide, narbonolide derivatives, and polyketides that are useful as antibiotics and as intermediates in the synthesis of compounds with pharmaceutical value.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2003:152931 USPATFULL  
TITLE: Recombinant narbonolide polyketide synthase  
INVENTOR(S): Ashley, Gary, Alameda, CA, UNITED STATES  
Betlach, Melanie C., San Francisco, CA, UNITED STATES  
Betlach, Mary, San Francisco, CA, UNITED STATES  
McDaniel, Robert, Palo Alto, CA, UNITED STATES  
Tang, Li, Foster City, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003104597	A1	20030605
	US 6902913	B2	20050607
APPLICATION INFO.:	US 2001-793708	A1	20010222 (9)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2000-657440, filed on 7 Sep 2000, PENDING Division of Ser. No. US 1999-320878, filed on 27 May 1999, PATENTED Continuation-in-part of Ser. No. US 1998-141908, filed on 28 Aug 1998, PENDING Continuation-in-part of Ser. No. US 1998-73538, filed on 6 May 1998, PENDING Continuation-in-part of Ser. No. US 1997-846247, filed on 30 Apr 1997, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-134990P	19990520 (60)
	US 1999-119139P	19990208 (60)
	US 1998-100880P	19980922 (60)
	US 1998-87080P	19980528 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Carolyn A. Favorito, Morrison & Foerster LLP, Suite 500, 3811 Valley Center Drive, San Diego, CA, 92130	
NUMBER OF CLAIMS:	20	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	6 Drawing Page(s)	
LINE COUNT:	4563	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 6 OF 7 USPATFULL on STN

TI DNA encoding methymycin and pikromycin  
AB A biosynthetic gene cluster for methymycin and pikromycin as well as a biosynthetic gene cluster for desosamine is provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2003:106911 USPATFULL  
TITLE: DNA encoding methymycin and pikromycin  
INVENTOR(S): Sherman, David H., St. Louis Park, MN, UNITED STATES  
Liu, Hung-Wen, Austin, TX, UNITED STATES  
Xue, Yongquan, St. Paul, MN, UNITED STATES

Zhao, Lishan, Carlsbad, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003073824	A1	20030417
APPLICATION INFO.:	US 2001-988384	A1	20011119 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. WO 1999-US14398, filed on 25 Jun 1999, UNKNOWN		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A., P.O. BOX 2938, MINNEAPOLIS, MN, 55402		
NUMBER OF CLAIMS:	60		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	164 Drawing Page(s)		
LINE COUNT:	10898		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 7 OF 7 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN'

TI Novel recombinant host cell (*Saccharopolyspora erythraea*) comprising recombinant biosynthetic pathways for producing precursor (butyryl CoA) required for biosynthesis of a product (propyl-6-deoxyerythronolide B); recombinant bacterium useful for antibiotic production

AN 2002-11559 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - A recombinant host cell (I) having one or more expression vectors expressing enzymes (II) capable of making product (P) and precursor (PR) required for biosynthesis of (P) in (I), where (I): (a) is unable to make (P) due to lack of all/part of a biosynthetic pathway required to produce PR; or (b) makes (P) in much smaller amounts due to PR being present in low amounts in the absence of (II), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a recombinant **polyketide synthase gene** (III) that encodes a loading **module** comprising a ketosynthase (KS)Q domain, an acyl transferase (AT) specific for ethylmalonyl CoA, and an acyl carrier protein (**ACP domain**); and (2) a host cell (IV) that comprises (III), and a recombinant gene such as recombinant *ccr* or *icm* genes.

WIDER DISCLOSURE - The following are disclosed: (1) a hybrid polyketide synthase (PKS) in which the loading **module** is composed of **KSQ domain**, an ethylmalonyl CoA specific AT domain, and an **ACP domain**, and AT domain specific for malonyl CoA; (2) recombinant DNA expression vectors and methods for making a polyketide and its required precursors in any host cell; (3) methods and genetic constructs for producing a glycosylated and/or hydroxylated polyketide compounds directly in the host cell of interest; (4) modified polyketide products of PKS which are further modified by hydroxylation and glycosylation reaction to exhibit antibiotic activity; and (5) novel ketolide compounds, polyketide compounds with potent antibiotic activity of significant interest due to activity against antibiotic resistant strain of bacteria.

BIOTECHNOLOGY - Preferred Host Cell: PR is preferably a primary metabolite that is produced in a first cell but not in a second heterologous cell. (I) comprises one or more expression vectors that drive expression of enzymes capable of making a product (polyketide, preferably propyl-6-deoxyerythronolide B (6-dEB) synthesized by modular polyketide synthase (PKS)) and a precursor (butyryl CoA) required for the biosynthesis of the product in the cell. Optionally, (I) is a *eryM* mutant producing a polyketide. Additionally, (I) comprises: (a) recombinant *ccr*, *acsA*, *bdh*, and *ech* genes; (b) recombinant *icm*, *vdh*, *ccr*, *acsA*, *vdh*, and *ech* genes; or (c) recombinant *icm*, *ccr*, *acsA*, *bdh*, and *ech* genes. Preferably propyl-6-dEB is produced by a modular PKS in a host cell comprising mutation in *eryM* gene, involving a precursor biosynthetic

enzyme such as propionyl CoA decarboxylase that converts propionyl CoA to methyl melanoyl CoA. The cell is preferably further modified to overexpress a biotin transferase enzyme encoded by the *birA* gene. (I) is optionally a *Streptomyces fradiae* cell expressing one or more genes encoding an erythromycin biosynthetic enzyme, and is producing 15-methylerythromycin.

ACTIVITY - Antimicrobial.

MECHANISM OF ACTION - Antibiotic. No suitable data given.

USE - (I) (*Saccharopolyspora erythraea* cell which does not express a functional *eryM* gene product) is useful for producing 14,15-propenylerythromycin and/or the corresponding 14,15-propenyl-6-deoxyerythronolide B. The method involves culturing (I) that expresses isobutyryl CoA mutase, valine dehydrogenase, butyryl CoA dehydrogenase, and 6-deoxyerythronolide polyketide synthase. The butyryl CoA dehydrogenase is expressed from gene isolated from *Clostridium acetobutylicum* or *Mycobacterium tuberculosis* (*fadE25*) (claimed). (I) is useful for producing polyketides (both macrolide aglycones and their modified derivatives) that are naturally occurring or produced by recombinant DNA technology. The polyketides produced are useful intermediates in formation of compounds with antibiotic or other activity through hydroxylation, epoxidation, and glycosylation reactions. The polyketides are useful as antibiotics and as intermediates in synthesis of other useful compounds such as erythromycin. The erythromycin analogs produced using (I) are used clinically as prokinetic agents to induce phase III of migrating motor complexes, to increase esophageal peristalsis, etc.

ADMINISTRATION - The polyketide compounds are administered orally, topically, parenterally or by inhalation spray. Dosages of the compound range from 0.01-50 (preferably 0.1-10) mg/kg body weight/day.

EXAMPLE - Construction of *eryM* knockout strains and production of 15-methyl-erythromycin was carried out follows. The construction of two recombinant DNA vectors designed to disrupt the *eryM* gene in *Saccharopolyspora erythraea* by single crossover was performed by the following method. These vectors can be used to generate a strain of *S.erythraea* that produces higher titers of 15-methyl erythromycin A or C than does wild-type *S.erythraea* under the same conditions without the need for the addition of an exogenous diketide. The desired strain differed from the wild-type strain in that intracellular pools of propanoyl-CoA were greatly reduced, pools of butanoyl-CoA were greatly elevated, and pools of methylmalonyl-CoA remain high. Disruption of the *eryM* gene, which encoded methylmalonyl decarboxylase, caused loss of erythromycin production that can be restored by feeding propionate, methylpropionate, or propanol in a wild-type strain of *S.erythraea*. The *S.erythraea eryM* gene was isolated by PCR or the coding region. An internal fragment of the *eryM* gene was isolated by polymerase chain reaction (PCR) and cloned into the *Xba*I and *Hind*III sites of the vectors pWHM3 (a *Streptomyces* vector) (conferred thiostrepton resistance) and pOJ260 (a *Streptomyces* vector) (conferred apramycin resistance) or gene disruption. The resulting vectors were propagated in *Escherichia coli* ET12567 to obtain unmethylated DNA. The above constructs were then introduced into a high-producing *S.erythraea* strain for gene disruption by homologous recombination. Protoplast transformation of this strain was very difficult, transformants were only obtained only using alkali-denatured, non-methylated DNA of only the pOJ260-derived construct. The transformant strains were grown for DNA isolation and in a standard two-stage shake flask fermentation procedure to evaluate production. Metabolites were quantitated by ion counting in a mass spectrometer relative to a roxithromycin internal standard. Putative *eryM* knockout transformants were shown to be correct by Southern blot hybridization. The mutant displayed the same morphology as the parent strain, both in liquid medium and on agar plates. The parent strain and two isolates of the *eryM*- mutant were grown using the shake flask procedure. In addition to the oil plus propanol feed, culture flasks were

fed equivalent levels of oil alone, oil plus butanol, oil plus propionate, and oil plus butyrate. The cultures were killed by the propionate and butyrate feeds, and these flasks were discarded. Samples were taken from other flasks each day and the set was analyzed by ion counting. Production of erythromycin A and B by the eryM- mutant was similar to that of the corresponding wild-type strain when fed oil alone or oil and propanol in rich medium. For both strains, production of erythromycin A and B was depressed with an oil and butanol feed. While knockout of eryM did not reduce production of erythromycin A and B in rich medium in the dramatic way. The high-producing wild-type strain appeared to produce low levels of 15-methyl-erythromycins when butanol was fed instead of propanol. The eryM- mutant produced a higher maximum percentage 15-methyl-erythromycin A and B with an oil and butanol feed compared to the wild-type strain, demonstrating that propionyl CoA levels were reduced in the eryM- strain. (85 pages)

ACCESSION NUMBER: 2002-11559 BIOTECHDS

TITLE: Novel recombinant host cell (*Saccharopolyspora erythraea*) comprising recombinant biosynthetic pathways for producing precursor (butyryl CoA) required for biosynthesis of a product (propyl-6-deoxyerythronolide B);  
recombinant bacterium useful for antibiotic production

AUTHOR: KATZ L; REVILL P

PATENT ASSIGNEE: KOSAN BIOSCIENCES INC

PATENT INFO: WO 2001031049 3 May 2001

APPLICATION INFO: WO 1999-US29447 25 Oct 1999

PRIORITY INFO: US 1999-161414 25 Oct 1999

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-256023 [30]